NDA 19-865/S-008 **AUG 23 1999**

Berlex Laboratories, Inc.
Attention: Ms. Nancy A. Konnerth
340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-2000

Dear Ms. Konnerth:

Please refer to your supplemental new drug application dated August 12, 1998 submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Betapace (sotalol) 80, 120, 160 and 240 mg Tablets.

We acknowledge receipt of your submission dated July 9, 1999.

This supplemental new drug application provides for final printed labeling revised as follows:

1. The following subsection has been added to the **DRUG INTERACTIONS** section:

> Antacids: Administration of BETAPACE within 2 hours of antacids containing aluminum oxide and magnesium hydroxide should be avoided because it may result in a reduction in Cmax and AUC of 26% and 20%, respectively and consequently in a 25% reduction in the bradycardic effect at rest. Administration of the antacid two hours after BETAPACE has no effect on the pharmacokinetics or pharmacodynamics of sotalol.

2. The word, “Mutagenicity” has been replace with, “Mutagenesis” in the **PRECAUTIONS** subsection title, “Carcinogenesis, Mutagenesis, Impairment of Fertility.”

3. The fifth paragraph under the **DOSAGE AND ADMINISTRATION** section has been changed from:

> Pharmacokinetic findings in patients requiring chronic hemodialysis is limited to six patients in two studies. In these patients, terminal elimination half life is prolonged to 40 hours in the interdialysis period and approached 7 hours during dialysis. It is estimated that 20%-40% of sotalol is removed during dialysis and that slight rebound of plasma concentration is noted post dialysis. Extreme caution must be taken in dosing patients in renal failure requiring hemodialysis, usual parameters of safety and efficacy (heart rate, QT interval and control of arrhythmia) must be closely monitored.

to:

> Extreme caution should be exercised in the use of sotalol in patients with renal failure undergoing hemodialysis. The half-life of sotalol is prolonged (up to 69 hours) in anuric patients. Sotalol, however, can be partly removed by dialysis with subsequent partial rebound in concentrations when dialysis is completed. Both safety (heart rate, QT interval) and efficacy (arrhythmia control) must be closely monitored.

4. The following have been returned to the **HOW SUPPLIED** section:

NDC 50419-109-10	120 mg strength, bottle of 100
NDC 50419-109-11	120 mg strength, carton of 100 unit dose

5. The phrase, “Caution: Federal law prohibits dispensing without prescription,” has been replaced with, “Rx only.”

We have completed the review of this supplemental application, and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the final printed labeling included in your July 9, 1999 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

If you have any questions, please contact:

Zelda McDonald
Regulatory Project Manager
(301) 594-5333

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
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